

## REMARKS

Upon entry of the above amendment, claims 37, 42, 44-49, 51, 55-58, 61, 63 and 65 will be pending in this application. Claim 54 has been canceled without prejudice. Claims 37, 56 and 61 have been amended. Support for the amended and new claims may be found throughout the specification and in original claims. For instance, support for claim 56 may be found, for example, on page 45 (line 20) to page 46 (line 18) of the specification. Support for amended claims 37 and 61 may be found, for example, on page 46 (line 19) to page 49 (line 27). Support for new claim 65 is supported, for example, on page 11 (line 7-17). No new matter has been added.

As a preliminary matter, Applicants acknowledge the Office Action's rejection of the pending claims for alleged nonstatutory double patenting over copending Application No. 09/315,581. As this rejection is provisional in nature, Applicants will address this issue in a subsequent response upon indication of otherwise allowable subject matter in the present application or in the 581 application.

The Office Action alleges that the present application is not entitled to the priority date of the 168 Application, because the 168 Application allegedly lacks the "substantive disclosure required for attaining priority..." Specifically, Examiner alleges that:

...the historical review of prior administration of various reagents (non-nucleic acid) to the lung is not a disclosure of the administration and subsequent lung delivery of aerosolized antisense oligonucleotides, nor of utilizing medical devices to perform such lung delivery...

Office Action at page 4; and

...the term inhalation, and pharmaceutical composition, does not substitute for the disclosure of lung delivery of antisense oligonucleotides using aerosolized or nebulized oligonucleotides.

Office Action at page 4.

Applicants respectfully disagree and assert that the present application is entitled to the priority date of the 168 Application under 35 U.S.C. 120. According to 35 U.S.C.

120, the present application is entitled to the priority date of the 168 Application if the 168 Application discloses the present invention (i.e., claims) in the manner provided by the first paragraph of 35 U.S.C. §112, which states:

The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full clear, concise, and exact terms as to **enable** any person skilled in the art to which it pertains... (emphasis added).

The 168 Application provides a written description for the presently pending claims that comports with the patent statutes. For example, claim 37 is directed to a method for administering oligonucleotides by aerosolizing the oligonucleotides and introducing the aerosolized oligonucleotides into the lung of a mammal. This claim is fully described by the 168 Application. For example, page 10 of the 168 Application clearly states that “oligonucleotides may be formulated in a pharmaceutical formulation” which may be administered *via inhalation*. In reading this disclosure, one of ordinary skill would know that such described oligonucleotide formulation for inhalation may be an aerosolized oligonucleotide formulation. Indeed, in his declaration filed December 18, 2001 in the present application, Dr. Gregory E. Hardee stated that prior to the November 20, 1991 priority date of the present application, the art pertaining to inhalation of therapeutics was well developed, and that aerosol therapy was known to those of skill in the art. As such, the language of the priority application cited above must be deemed a description of a method of administering oligonucleotides by aerosolizing them and introducing them into the lung.

Moreover, the described method of administering oligonucleotides via inhalation by, for example, aerosolizing the oligonucleotides, is fully enabled. As discussed above, Dr. Hardee states in his declaration that aerosol therapy was known to one of ordinary skill in the art prior to the filing date of the 168 Application, and that “the art pertaining to inhalation therapeutics was well developed, and those skill in the art at the time knew how to formulate and deliver a wide variety of compositions for therapeutic and/or diagnostic purposes.” See Declaration filed on December 18, 2001. Thus, the 168

Application is fully enabling with respect to the described method of administering oligonucleotides via inhalation by, for example, aerosolizing the oligonucleotides.

In view of the preceding remarks, Applicants respectfully request reconsideration and granting of their claim for priority with respect to the 168 Application.

Claims 37, 42, 44-49, 51, 54-58, 61 and 63 are rejected for alleged indefiniteness under 35 U.S.C. §112, second paragraph. With regard to claim 37, the Office Action has requested clarification of the language:

... wherein the sugar moiety of at least one nucleoside unit of said antisense oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage within said antisense oligonucleotide is not a phosphodiester or a phosphorothioate linkage.

With respect, it is believed that the language is clear to those of skill in the art. An oligonucleotide in accordance with claim 37 is an oligonucleotide wherein either (1) at least one of the sugar moieties of the oligonucleotide is other than a 2'-deoxyribofuranosyl sugar moiety; or (2) the oligonucleotide contains at least one internucleotide linkage that is other than a phosphodiester or a phosphorothioate linkage. Thus, one example of an oligonucleotide of the claims would be an oligonucleotide having, for example, 8 nucleosides, wherein one of the nucleosides does not comprise a 2'-deoxyribofuranosyl sugar moiety, but comprises a different sugar moiety, for example, a 2'-O-substituted ribofuranosyl sugar moiety. Another example of an oligonucleotide of the claims would be an oligonucleotide having, for example, 10 nucleotides, wherein one of the internucleotide linkages is not a phosphodiester linkage or a phosphorothioate linkage, but is instead a different linkage, for example, a 3'-methylenephosphonate linkage. Inasmuch as those of skill in the art would understand that language of the claims, Applicants respectfully assert that the claim language is proper.

Claim 42 is rejected for alleged improper dependency from claim 39. Applicants note that the recited claim 42 actually depends from claim 37, and this dependency is believed to be proper.

Claim 56 is rejected for allegedly being unclear with respect to the recitation of an animal suspected to suffer from a disease or disorder. For clarity, claim 56 has been

amended to recite that the disease or disorder is one which may be treated or diagnosed by the administered antisense nucleic acids.

In view of the preceding remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §112, second paragraph.

Claims 37, 42, 44-49, 51, 54-58, 61 and 63 are rejected under 35 U.S.C. 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to show possession by the inventors when the application was filed. Specifically, Office Action appears to assert that the Applicants were not in possession of the claimed invention because the “specification and claims do not indicate the distinguishing features and attributes that are concisely shared by genus members...” Thus, as best understood, the Office Action appears to assert that the description is lacking because the specific structures of the possible oligonucleotides amenable to the present methods are not set forth. With respect, Applicants are not aware of any such requirement in the patent laws.

Significantly, Applicants note that the Office Action states on page 7 that the claims are drawn to antisense oligonucleotides. However, and with respect, the present claims in fact recite *methods of administration* of antisense oligonucleotides (claims 37, 42, 44-49, 51, 54-58) and *medical devices for pulmonary delivery of aerosols* comprising antisense oligonucleotides (claims 61 and 63). The claims do *not* recite the antisense compounds *per se*. A wide variety of antisense oligonucleotides are amenable to the claimed methods and devices, and Applicants are entitled to obtain a patent commensurate in scope with their invention. Contrary to the apparent assertion of the Office Action, Applicants are not aware of any requirement in the patent laws mandating that Applicants claiming a method generally amenable to delivery of a variety of therapeutics set forth the specific identity of each of the therapeutics in the claims. Should the Office persist in the present rejection, Applicants respectfully request that such authority be provided.

Moreover, and also contrary to the assertions of the Office Action, the claims and the specification set forth a legally sufficient description of the antisense compounds described in the claims. As discussed above, the specification and pending claims

describe and recite methods for administering antisense oligonucleotides wherein either (1) at least one of the sugar moieties of the oligonucleotide is other than a 2'-deoxyribofuranosyl sugar moiety; or (2) the oligonucleotide contains at least one internucleotide linkage that is other than a phosphodiester or a phosphorothioate linkage. Also as discussed above, those of skill in the art would understand this language, especially in view of the present specification, and the Office Action has presented no evidence to the contrary. Accordingly, it is not seen how the present claims can be said to lack an adequate written description.

In view of the preceding remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Claims 37, 42, 44-49, 51, 54-58 and 61 are rejected for allegedly anticipation under 35 U.S.C. 102 (e) by U.S. Patent No. 5,733,572 to Unger (hereinafter "Unger").

As a preliminary matter, Applicants reassert that the present application is entitled to the priority date of the 168 Application, as discussed above, which is prior to the November 29, 1994 filing date of Unger. Thus, Unger is not properly cited as prior art against the claims of the present application.

Moreover, Applicants assert that even if Unger is properly cited, it cannot anticipate the present claims, because it does not disclose all the elements of the claims thereof. For example, amended claim 37 recites that the aerosolized composition comprises liquid particulates or solid particulates. On the other hand, Unger reports gas filled liposomes which often takes the visual form of a foam. In particular, the Unger liposomes are microspheres filled with gas and/or gaseous precursors. As described on page 47-49 of the present specification, the aerosolized liquid particulates and the solid particulates of the present invention are not gas filled liposomes. Rather, for example, the liquid particulates of the present invention comprise primarily water and an oligonucleotide. Thus, Unger cannot anticipate the present invention because it does not disclose the aerosolized solid or liquid particulates of the present invention.

Claim 63 is rejected for allegedly obviousness under 35 U.S.C. 103 (a) over Unger in view of U.S. Patent No. 5,514,788 to Bennett (hereinafter "Bennett"). As a preliminary matter, Applicants again assert the Unger patent is not prior art against the

claims of the present application. Nevertheless, even if Unger were properly cited, the combination of Unger and Bennett still would not produce the presently claimed invention.

It will be appreciated that Claim 63 depends from claim 37, and therefore contains all the elements of claim 37. As discussed above, Unger does not disclose or teach all the elements of claim 37. Thus, Unger also does not disclose or teach all the elements of claim 63. For example, Unger does not disclose or teach that the aerosolized composition of claim 63 comprise a liquid particulate or a solid particulate. Bennett, alone or in combination with Unger, does not cure this deficiency, and in fact, Bennett is devoid of any disclosure or teaching of aerosolized compounds. Therefore, the combination of the cited art neither discloses nor suggests the presently claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Applicants submit that pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,



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